

## The Potential of Topical Imiquimod

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## Editorial

Imiquimod [1-(2-methylpropyl)-1H-imidazo [4,5-c] quinolin-4 amine] is imidazoquinolineamine [1,2] and has a molecular formula of  $C_{14}H_{16}N_4$  [2,3]. The Molecular weight of Imiquimod is 240-260 kDa [3,4], and its molecular mass is 240.304 g/mol [2]. Imiquimod is an immune response modulator and a Toll Like Receptor (TLR) agonist [2]. Imiquimod affects the production of Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) [5-7], granulocyte-colony stimulating factor (G-CSF) [6], Macrophage Inflammatory Protein (MIP)-1 [5-7], Monocyte Chemo attractant Protein (MCP)-1 [5-7], interleukin (IL)-1 [4,7], IL-1receptor antagonist [7,8], IL-5[7], IL-6 [5, 6, 9-11], IL-8 [5,6,10], IL-10 [5,6], IL-12 [7], interferon (IFN)- $\alpha$  [5,6,10,11,12], IFN- $\beta$  [4], IFN- $\gamma$  [1,7], tumor necrosis factor (TNF)- $\alpha$  [5,6,9-15], and apoptosis through FasR/Fas ligand [13-15] and migration of Langerhans Cells (LCs) [11-16,17] in mouse or *in vitro* model.

Eleven TLRs have been identified in the human body, and TLR7 and -8 bearing LCs play some roles in imiquimod-induced immune response [2,18]. Imiquimod induce antitumor or antiviral activity [5,19] through direct or indirect actions [20]. Direct actions are caused by TLR binding macrophages, LCs (dendritic cells) and monocytes [20,21]. Imiquimod stimulates the ability of LCs to present antigen [5,22] and enhances LCs migration [16,20]. Indirect actions are caused by some cytokines [20]. The primary cytokines that increase cytotoxic T cells and NK cells are IL-12, TNF- $\alpha$  and IFN- $\gamma$ . These actions induce the blocking of angiogenesis [23,24] and the stimulation of antitumor T cells [25]. The effects of imiquimod then inhibit tumor progression.

Previous studies have described imiquimod used to treat some dermatoses, keratoacanthoma [23], actinic keratosis [10,26-32], Bowen's disease [32-34], squamous cell carcinoma [10,15,32,35-37], basal cell carcinoma [2,10,18,21, 25-27,32-38,39], malignant melanoma [10,27,40,47], EM Paget's disease [10,41,42], cutaneous T cell lymphoma [10,43], Kaposi sarcoma [10], Merkel cell carcinoma [44], genital herpes [27], alopecia areata [27], psoriasis [27] and molluscum contagiosum [27]. The mechanisms through which imiquimod induces immune reactions are interesting, and many dermatologists have proposed that imiquimod could be used in other dermatoses. Gibert [45] reported that the herpes simplex virus 2 infection which was not responded to antiviral medicines in an AIDS patient was treated successfully by imiquimod. Imiquimod has the potential to be an effective treatment not only for some kinds of skin tumor, but also for intractable cases of dermatoses, mucous membrane diseases and other organ tumors (early stage)under conventional treatments.

The adverse effects at the application sites are erythema, erosion, vesiculation, itching and pain. The most frequent adverse effect is erythema with pain at the application site, and this reaction could be an aspect of effect. Systemic rare adverse effects were fatigue, headache, diarrhea and fever [46].

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